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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/665,350	09/18/2000	Avi Ashkenazi	10466/14	8200

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EXAMINER	
CHERNYSHEV, OLGA N	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 06/23/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/665,350	ASHKENAZI ET AL.	
	Examiner	Art Unit	
	Olga N. Chernyshev	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 May 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *39-46 and 49-51* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *39-46 and 49-51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

9.00

DETAILED ACTION

Response to Amendment

1. Claims 39-44 have been amended as requested in the amendment filed on May 06, 2005. Claims 39-46 and 49-51 are pending in the instant application.

Claims 39-46 and 49-51 are under examination in the instant office action.

2. The Text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. Any objection or rejection of record, which is not expressly repeated in this action has been overcome by Applicant's response and withdrawn.

4. Applicant's arguments filed on May 06, 2005 have been fully considered but they are not deemed to be persuasive for the reasons set forth below.

Claim Rejections - 35 USC § 101

5. Claims 39-46 and 49-51, as amended, stand rejected under 35 U.S.C. 101 because the claimed invention is drawn to an invention with no apparent or disclosed specific and substantial credible utility for reasons of record in previous office actions of record.

Applicant traverses the rejection by addressing the issues related to the asserted utility of the clamed polypeptides as markers for lung and colon tumors. At pages 6-8 of the Response, Applicant reviews the Utility Examination Guidelines, case law pertained to utility and appropriate sections of MPEP. Applicant's review of the issue of utility, the case law that has been cited and the holding that is found in that case law is not disputed. The only point of

disagreement appears to be the interpretation of what constitutes a specific, substantial and credible utility.

At page 9 of the Response, Applicant submits that "[t]able 8 explicitly states that PRO187 is significantly overexpressed in lung and colon tumors as compared to the normal control. [...] The above disclosure is sufficient to establish a specific, substantial and credible utility for the PRO187 polypeptide". The Examiner maintains the position that gene amplification of polynucleotides encoding PRO187 of SEQ ID NO: 23 in primary samples of lung and colon cancer, as indicated in Table 9 on pages 230-234 of the instant specification, is not predictive of increased amounts of polypeptide of SEQ ID NO: 23, and, therefore, the polypeptide of SEQ ID NO: 23 could not be used as a marker for lung and colon cancer without further and significant amount of experimentation.

Applicant refers to publications of Ortnoft et al., Hayman et al. and Pollack et al. to support the position that proteins expressed by genes that are amplified in tumors can be used as markers for cancer and states that "it is more likely than not" that a gene which is amplified in tumor cells will have increased gene expression" (middle at page 11 of the Response). Applicant's arguments have been fully considered but are not persuasive for the following reasons.

The full analysis of the publications submitted with the reply filed on October 08, 2004, was presented in the previous office action of record. To summarize, publications of Orntoft et al., Hayman et al. and Pollack et al. (1) are mostly limited to the analysis of correlation between increased copy of DNA and corresponding amount of mRNA, which is not relevant in the instant case to support the correlation between DNA and protein levels; (2) explain that cases when

copy of DNA is amplified less than 2-fold, which is 4 out of 5 cases of colon cancer samples in the instant case of polypeptide of SEQ ID NO: 23 (see Table 9), are considered "at the border of detection" (page 43, second column and also page 37, top of the second column of Orntoft et al. paper); (3) clearly caution regarding limitations of gene expression pattern analysis, "[d]espite this progress in diagnostic classification, the molecular mechanisms underlying gene expression patterns in cancer have remained elusive, and the utility of gene expression profiling in the identification of specific therapeutic targets remained limited" (Hayman et al., page 6240, first column).

Regarding the merit of the argument, even if to assume that the increase of DNA copy correlates with the increase of the amount of corresponding protein, there appears to be no evidence or scientific reasoning presented to conclude that such increase is directly proportional to the amount of number of copies of DNA, the only information available from the instant specification, as filed. Applicant submits that "it is not a legal requirement to establish a "necessary" correlation between an increase in the copy number of the mRNA and protein expression levels that would correlate to the disease state or that it is "imperative" to find evidence that protein levels can be accurately predicted" (middle at page 14 of the Response). However, in view of total absence of the biological significance of the polypeptide of SEQ ID NO: 23 in lung and colon cancer, recognition of "a positive correlation" between marginally overexpressed DNA in a limited number of lung and colon cancer tissue samples is only suitable for further research to establish if and what amount of the polypeptide of SEQ ID NO: 23 is diagnostic for what type of lung or colon cancer. It is a matter of law that the claimed invention

must be useful in currently available form, which precludes any further experimentation to establish the utility of the claimed invention.

Applicant's asserted utility for the polypeptide of SEQ ID NO: 23, particularly in view of lack of knowledge as to the biological function of the polypeptide of SEQ ID NO: 23 with respect to lung or colon cancer, the type of cancer which can be diagnosed, and how much of the polypeptide of SEQ ID NO: 23 is indicative of disease, constitutes a utility that requires further research to identify or reasonably confirm a "real world" context of use. See *Brenner v. Manson*, 148 U.S.P.Q. 689 (Sus. Ct, 1966). This type of utility is not considered a "substantial utility". Thus, for the reasons set forth, the claimed polypeptides do not have a real-world use and do not meet the utility requirements under 35 USC 101.

Claim Rejections - 35 USC § 112

6. Claims 39-46 and 49-51 stand rejected under 35 U.S.C. 112, first paragraph for reasons of record in previous office actions of record. Specifically, since the claimed invention is not supported by either a clear asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

7. Claims 39-43, as amended, stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for reasons fully expalined in previous office actions of record.

Applicant submits that "the genus of **native polypeptide sequences** with at least 80% sequence identity to SEQ ID NO: 23, and which possess the functional property "wherein the nucleic acid encoding said polypeptide is amplified in lung or colon tumors" would meet the requirement of 35 U.S.C § 112, first paragraph, as providing adequate written description" (bottom at page 17 of the Response). Applicant further argues that "[o]ne of skill in the art could readily test these variant native polypeptide sequences to determine whether its encoding nucleic acid is amplified in lung or colon tumors based on step-by-step methods set forth throughout the specification and Example 90" (middle at page 18). Applicant's arguments have been fully considered but are not deemed to be persuasive for the following reasons.

Applicant is advised that addition of limitation "native sequence" to the claimed genus of polypeptides did not obviate the instant rejection of record because the instant claimed genus of polypeptides having structural similarity to the only disclosed polypeptide of full sequence of SEQ ID NO: 23, wherein the nucleic acid encoding said polypeptide is amplified in colon and lung tumors, is not disclosed in the instant specification, as filed. Based on the information presented in the instant specification, one skilled in the art clearly cannot envision the claimed polypeptides (those polypeptides, which are 80%, 85%, 90%, 95% and 99% identical to an amino acid sequence having SEQ ID NO: 23, which are encoded by a nucleic acid amplified in lung or colon tumors) because there is no disclosure of complete structure of the claimed polypeptides, or structure/function correlation or any combination of the above. *Vas-Cath Inc. v. Mahurkar*, 19USPQ2d 1111, makes it clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now*

claimed." (See page 1117.) In the instant case the only polypeptide that is fully disclosed in the instant specification that meets the written description requirement is the polypeptide of SEQ ID NO: 23. Applicant is advised that "make and test" approach such as to test if a polypeptide that has, for example, 80% structural similarity to the polypeptide of SEQ ID NO: 23 is also encoded by the nucleic acid amplified in colon or lung tumors to meet the limitations of claim 39, is not probative to satisfy the written description inquiry. It is not the ability of one skilled in the art to experiment which polypeptides are encompassed by claims 39-43 but the specification itself that must describe the claimed genus of polypeptide in clear and concise form to meet the requirements of 35 U.S.C § 112, first paragraph.

Conclusion

8. No claim is allowed.

9. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Olga N. Chernyshev whose telephone number is (571) 272-0870. The examiner can normally be reached on 8:00 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony C. Caputa can be reached on (571) 272-0829. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Certain papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax center located in Crystal Mall 1 (CM1). The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers.

Official papers filed by fax should be directed to (703) 872-9306. If this number is out of service, please call the Group receptionist for an alternative number. Faxed draft or informal communications with the examiner should be directed to (571) 273-0870. Official papers should NOT be faxed to (571) 273-0870.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Olga N. Chernyshev, Ph.D.
Primary Examiner
Art Unit 1646

June 15, 2005